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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/741,534	12/19/2003	Alain Baron	18528.675 / 0218-UTL-9	5134

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Intellectual Property Department
Amylin Pharmaceuticals, Inc.
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EXAMINER	
STOICA, ELLY GERALD	
ART UNIT	PAPER NUMBER
1647	

MAIL DATE	DELIVERY MODE
08/18/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/741,534	BARON ET AL.	
	Examiner	Art Unit	
	ELLY-GERALD STOICA	1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,2,7-11,16-18,28,29,34-38,43-45,52,53,55 and 56* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,2,7-11,16-18,28,29,34-38,43-45,52,53,55 and 56* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *03/14/2008; 06/20/2008*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Status of the claims

1. Applicant, in the reply filed on 05/06/2008, cancelled claims 4-6, 13-15, 31-33, 40- 42, 46-51, and 54 and amended claims 1, 6-7, 10, 28, and 37. Thus, claims 1, 2, 7-11, 16-18, 28-29, 34-38, 43-45, 52-53 and 55-56 are pending.

Information Disclosure Statement

2. The information disclosure statement (IDS) submitted on 03/14/2008 is in compliance with the provisions of 37 CFR 1.97. Accordingly, the information disclosure statement is being considered by the examiner.

The information disclosure statement filed 06/20/2008 fails to comply with the provisions of 37 CFR 1.97, 1.98 and MPEP § 609 because the reference cited is irrelevant to the subject matter of the instant Application. It has been placed in the application file, but the information referred to therein has not been considered. Applicant is advised that the date of any re-submission of any item of information contained in this information disclosure statement or the submission of any missing element(s) will be the date of submission for purposes of determining compliance with the requirements based on the time of filing the statement, including all certification requirements for statements under 37 CFR 1.97(e). See MPEP § 609.05(a).

Withdrawn claim rejections

Claim Rejections - 35 USC § 112

3. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

The rejection of claims 1, 2, 7-11, 16-18, 28-29, 34-38 and 43-45 under 35 U.S.C. 112, first paragraph, is withdrawn in view of the amendments to the claims.

Maintained claim rejections

Claim Rejections - 35 USC § 102

4. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

5. Claims 1-2, 7, 10, 11, 16, 28, 29, 34, 37, 38, 43, 52-53, and 55-56 remain rejected under 35 U.S.C. 102(b) as being anticipated by Momose et al. (U.S. Pat No. 6,251,926) for the reasons of record.

Momose et al. teach a method of treating diabetic late complications (including nephropathy, hypertension, neuropathy, and retinopathy) using GLP-1 (7-37), in a combination with other drugs, orally or parenterally (injection) (col. 23, lines 6-65; col. 24, lines 54-56; col. 25, lines 1-2; col. 18, lines 26-39).

Since the method of treatment in the claims of the instant application **comprises** administering GLP-1, the claims are anticipated by Momose et al.

On page 6 Applicants argue the Patent to Momose et al. is not enabled for treating nephropathy because the GLP-1 is mentioned in long “laundry list" of compounds for treating diabetes mellitus.

The arguments were carefully considered but not found persuasive because as mentioned supra, the method of treatment in the claims of the instant application **comprises** administering GLP-1. As such, a person of ordinary skill in the art, by practicing the method of treatment of Momose et al., would have necessarily practice the claimed invention, since the property of GLP-1 would not have changed on the basis of the condition being treated. The fact that Momose et al. mention numerous conditions to be treated is not pertinent. Applicants argue that Momose provides no reasonable expectation of success; however, the mere suggestion is, in this case, enough. Should applicants argue that Momose is not enabling, the Examiner would have to re-consider a rejection of the instant claims under 35 U.S.C. §112, first paragraph.

Applicant is also arguing that it would require undue experimentation to find the claimed invention by following the teachings of Momose et al. and thus the reference is not enabling.

The arguments were carefully considered but not found persuasive because there is a long felt need for treatment of diabetes, and Momose presents a finite number of solutions for doing so, and is therefore enabling.

6. Claims 1-2, 7, 10-11, 16, 28-29, 34, 37-38, 43, 52-53 and 55-56 remain rejected under 35 U.S.C. 102(e) as being anticipated by Knudsen et al.(US 20030144206, 12/23/2002) for the reasons of record.

On page 7 Applicants argue that Knudsen et al. is not prior art to the presently claimed invention because Knudsen et al. was filed on Dec, 23, 2002, but the present invention claims priority to the provisional application Serial No. 60/434,888, filed Dec. 19, 2002.

The arguments were carefully considered but not found persuasive because, according to MPEP § 706.02 (f) (1), the 35 U.S.C. 102(e) date of a reference is the earliest effective filling date taking into consideration any proper benefit claims to prior U.S. applications under 35 U.S.C. 119(e) or 120, which for Knudsen et al. is 01/17/2002 (the date of filling the provisional Application 60/350087). Therefore, Knudsen et al. is a valid 102 (e) reference and the rejection is maintained.

Claim Rejections - 35 USC § 103

7. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

8. Claims 8-9, 17-18, 35-36 and 44-45 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Momose et al. (U.S. Pat No. 6,251,926) for the reasons of record.

The rejected claims add specific dosage limitations. As iterated supra, since the method of treatment in the claims of the instant application **comprises** administering GLP-1, the teachings of Momose et al. are valid for the instant Application. Although Momose et al. teach throughout that therapeutic dosage amounts of the compounds are to be administered, they do not expressly teach the same in terms of μg/kg/day or mg/day of the rejected claims of the instant Application.

However, it would have been obvious to one of ordinary skill in the art at the time the invention was made to use any therapeutic effective amount of the compounds used Momose et al., including dosage and the regimen disclosed by Applicant, because the reference teaches the advantageous use of the same routes of administration (oral or parenterally (injection)) and that it be administered in any therapeutic amount thereof. One of ordinary skill in the art would be motivated to arrive at the present range or specific amounts therein, simply by routine optimization taking into consideration the patient in question and the other factors impacting treatment. Also, given the breadth of the ranges in the claims, there does not appear to be any criticality, and that the claims are inviting the artisan to do the same kind of experimentation that the reference would require. From the teachings of the reference, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was prima facie obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the reference.

The Examiner's position is supported by the case law:

In re Boesch, 617 F.2d 272,276, 205 USPQ 215, 219 (CCPA 1980).

"discovery of an optimum value of a result effective variable in a known process is ordinarily within the skill of the art."

See also Merck & Co. v. Biocraft Labs. Inc., 874 F.2d 804, 809, 10 USPQ2d 1843, 1847-48 (Fed. Cir. 1989)

Merck & Co. v. Biocraft Labs. Inc., 874 F.2d 804, 809, 10 USPQ2d 1843, 1847-48 (Fed. Cir. 1989)

determination of suitable dosage amounts in diuretic compositions considered a matter of routine experimentation and therefore obvious.

9. Claims 6, 8-9, 17-18, 35-36 and 44-45 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Knudsen et al. (US 20030144206, 12/23/2002) for the reasons of record.

Contrary to Applicants arguments, from page 7, Knudsen et al. is a valid prior art reference (see supra) and thus the rejection is maintained.

10. Claims 1-2, 7-11, 16-18, 28-29, 34-38, 43-45, 52-53 and 55-56 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Coolidge et al. (WO 01/89554, 11/29/2001), in view of Holst et al. (WO 02/085406, 04/24/2002) and in further view of Guitard et al. (US 2001/0016586, 08/23/2001) for the reasons of record.

On page 9, Applicants argue that the rejection over Coolidge in view of Hoist and Guitard would not lead the person of ordinary skill in the art to the treatment of a nephropathy or end stage renal disease by administration of GLP- 1, or whether the references would lead the person of ordinary skill to believe that GLP-1 can be administered to reduce proteinuria, or prevent or slow the progression of glomerulosclerosis. Further, Applicant alleges that there is no rational basis to support the rejection.

The arguments were carefully considered but not found persuasive because the GLP-1 molecule of the invention of Coolidge et al. would bind and exert its action irrespective of the condition sought to be treated. Further, Coolidge et al. which clearly show that excess glucagon may lead to myocardial tissue damage and GLP-1, which is an antagonist, was used to treat an ischemic patient which was incapable of auto-regulation of blood glucose. The same mechanism of action is present in the renal tissue, where excess glucose due to the diabetes will damage the renal cells and lead to nephropathies and may lead to ESRD.

GLP-1 and analogs were previously known in the art for their use to treat diabetes, as admitted by the Applicant in the specification. The definition of the ESRD, end-stage renal disease clearly presents diabetes and hypertension as an etiological cause for the disease. Both diabetes and hypertension can be treated by GLP-1, as proved by Holst et al. Holst et al. teach treating insulin resistance-associated conditions with GLP-1 (p. 4, lines 6-10). Manifestations of the insulin resistance syndrome include hypertension albuminuria both related to renal function.

Guitard et al. teach the use of GLP-1, as a hypoglycemic agent, in nephropathies, peripheral angiopathies, hypertension, microangiopathic changes, diabetes and insulin resistance.

This is why, when all the cited references are considered as a whole, it would have been obvious for a person of ordinary skill in the art at the time that the invention was made to combine the teachings of Coolidge et al. with the teachings of Holst et al and Holst et al. to treat nephropathy patients with a reasonable expectation of success because Coolidge et al. treats ischemic heart disease with GLP-1 and thus inherently blocks the action of glucagon and treats insulin resistance as, taught by Holst et al. The expectation of success is reasonable when combined Guitard's et al. teachings of using GLP-1 in nephropathies.

On page 9 Applicants argues that there is no motivation to combine the references. The arguments were carefully considered but not found persuasive because , the motivation is always present to a skilled artisan that uses known options available to him to optimize a process or a formulation, as eloquently expressed in the Supreme Court decision in KSR International Co. v. Teleflex Inc., 550 US, 82 USPQ2d 1385 (2007). The person of ordinary skill in the art, having the walls of the laboratory hung with the cited art, would have been motivated to combine the references in the same manner cited in the rejection.

In response to applicant's argument that the examiner's conclusion of obviousness is based upon improper hindsight reasoning, it must be recognized that any judgment on obviousness is in a sense necessarily a reconstruction based upon hindsight reasoning.

But so long as it takes into account only knowledge which was within the level of ordinary skill at the time the claimed invention was made, and does not include knowledge gleaned only from the applicant's disclosure, such a reconstruction is proper. See *In re McLaughlin*, 443 F.2d 1392, 170 USPQ 209 (CCPA 1971).

Conclusion

11. No claims are allowed.

12. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to ELLY-GERALD STOICA whose telephone number is (571)272-9941. The examiner can normally be reached on 8:30-17:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Manjunath N. Rao can be reached on (571) 272-0939. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Lorraine Spector/ Ph.D.

Primary Examiner, Art Unit 1647